Absence of *Twisted Gastrulation* (*Twsg1*) Limits the Population of Cranial Neural Crest Cells

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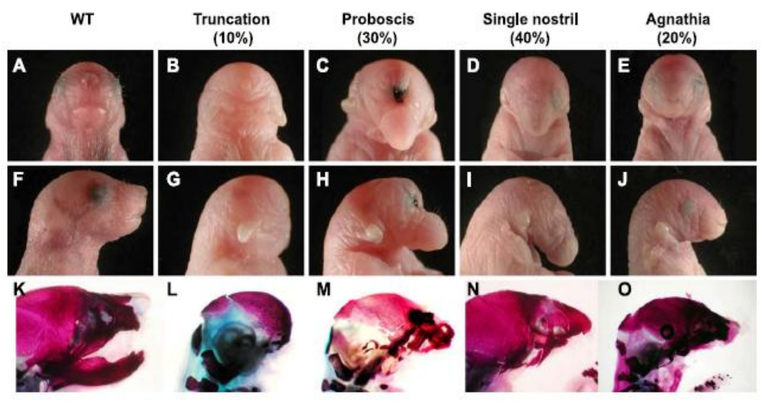
Twsg1 affects craniofacial development

•Craniofacial defects are a very common birth defect.

•*Twsg1*$^{-/-}$ mutants have craniofacial abnormalities, including altered derivatives of the first branchial arch (BA1).

•Twsg1 is involved in craniofacial development by regulating bone morphogenetic protein (BMP) signaling in the medial region of BA1.

Variable Phenotypes in *Twsg1*$^{-/-}$ mutants



Twsg1 impacts neural crest cells (NCCs)

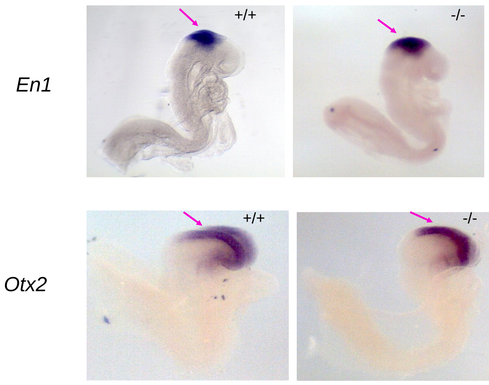
•NCC migrate from the posterior midbrain (mesencephalon) to the medial region of BA1 that gives rise to most of the mandible.

•Defects in BA1 may be due to defects in NCCs.

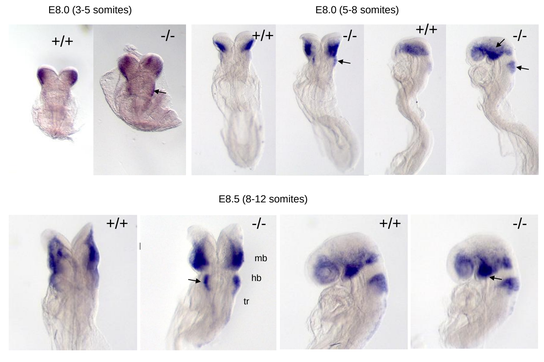
The goal of this project was to study NCC population in *Twsg1*$^{-/-}$ mice. The hypothesis was that the midbrain formation might be abnormal and/or NCC marker expression would be decreased.

Results

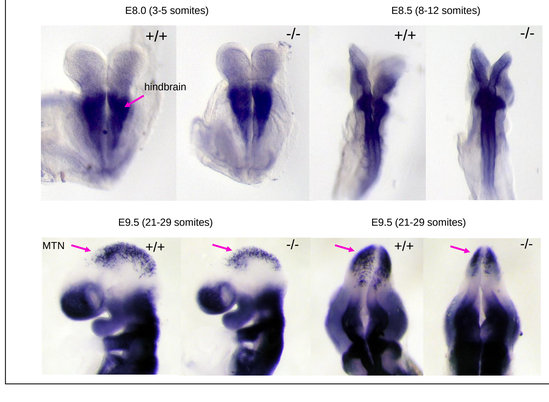
Midbrain specification is normal in *Twsg1*$^{-/-}$ mice at E8.5.



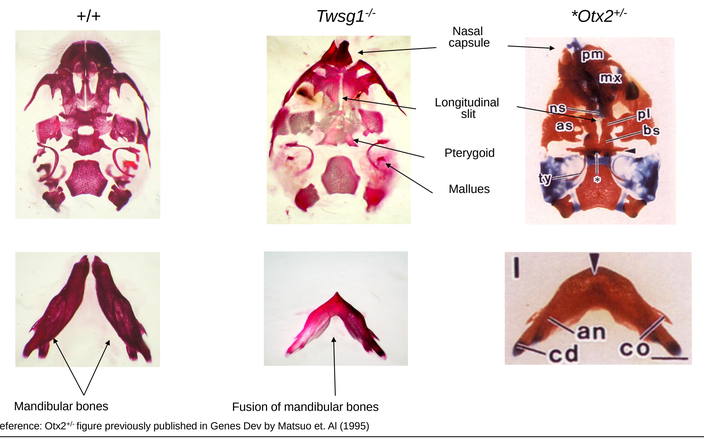
As shown by *Sox10* expression, NCC generation is not reduced in *Twsg1*$^{-/-}$ embryos at E8-E8.5



Expression of NCC marker *Crabp1* is normal at E8-E8.5, but reduced in mesencephalic trigeminal neurons (MTN) at E9.5



Similar ventral skull defects are present in *Twsg1*$^{-/-}$ and *Otx2*$^{+/-}$ mutants. *Otx2*$^{+/-}$ mice lack midbrain NCC-derived skeletal elements, suggesting Twsg1 may be functioning in similar areas.



*Reference: Otx2$^{+/-}$ figure previously published in Genes Dev by Matsuo et. Al (1995)

Conclusions

•The NCC population is not decreased at E8.0 or E8.5 but derivatives of NCCs are reduced at E9.5.

•The NCC population is likely being depleted at a point between E8.5 and E9.5, for example through increased apoptosis or reduced proliferation.

Future Goals

•Future research will directly assess proliferation, apoptosis, and BMP signaling in NCC populations in the absence of *Twsg1*.

•The NCC population will be studied between E8.5 and E9.5 so that the limiting of the population can be better understood.

References

MacKenzie, B., Wolff, R., Lowe, N., Billington Jr, C.J., Peterson, A., Schmidt, B., Graf, D., Mina, M., Gopalakrishnan, R., Petryk, A., 2009. Twisted gastrulation limits apoptosis in the distal region of the mandibular arch in mice. Dev. Biol. doi:10.1016/j.ydbio.2008.12.041.

Petryk, A., Anderson, R.M., Jarcho, M.P., Leaf, I., Carlson, C.S., Klingensmith, J., Shawlot, W., O'Connor, M.B., 2004. The mammalian twisted gastrulation gene functions in foregut and craniofacial development. Dev. Biol. 267, 374-386.